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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/640,780	08/18/2000	Jacques Dumas	BAYER8C1	7350

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	26

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/640,780	Applicant(s) DUMAS ET AL.	
	Examiner Binta M. Robinson	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,11-13,15,16,37,41-43,46 and 80* is/are pending in the application.

4a) Of the above claim(s) *41 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9,11-13,15,16,37,41,43,46 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

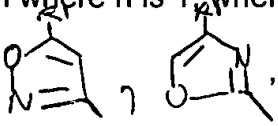
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *18*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detail d Action

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9,11,12, 13,15,16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1, 2, 9, 11, 13 of copending Application No. US 1997-995750. Although the conflicting claims are not identical, they are not patentably distinct from each other because US 1997-995750 claims a method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I where B is aryl substituted by Xn where n is 1, where X is –Y-Ar where Y is O or S, and Ar is phenyl or pyridinyl and A is  , wherein R1 is selected fro the group consisting of halogen, C3-C10 alkyl, C3-C10 cycloalkyl, C1-C13 heteroaryl, C6-14 alkaryl, up to per –halosubstituted C1-C10 alkyl, up to per –halosubstituted C3-C10 cycloalkyl, up to per-halosubstituted C1-C13 heteroaryl, up to per-halosubstituted C6-14 aryl, and up to per-halosubstituted C7-24 alkaryl, Rc is hydrogen, halogen, C1-C10 alkyl, up to per-halosubstituted C1-C10 alkyl or combines with R1 and the ring carbon atoms to which

R1 and Rc are bound to form a 5- or 6-membered cycloalkyl, aryl or hetaryl ring with 0-2 members selected from O, N and S. The difference between the US 1997-995750 method of treating and the instantly claimed method of treating is the teaching of a method of treating diseases other than cancer mediated by p38 with the instant compounds rather than a method of treating cancerous cell growth with a subgenus of the instant compounds of formula I. p38 has been found to be involved in inhibiting cell proliferation. (See Reference U), In view of Blanco, (See Reference U), it would have been obvious to one of ordinary skill in the art to treat diseases mediated by p38 other than cancer with a subgenus of the instant compounds of formula I. For instance, see the method of treating a disease other than cancer mediated by p38, with a compound, Urea, N-[5-(1,1-dmethylethyl)-3-isoxazoyl]-N'-[4-(4-hydroxyphenoxy)phenyl]. Accordingly, the method of treating cancerous cell growth with the instant compounds is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed method over those of the US 1997-995750 .

2. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 37 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 35 of copending Application No. US 1997-995750. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9, 11, 12, 13, 15, 16, 37, 43, and 46 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 11, 12, 13, 15, 16, 37, 43, 46 of copending Application No. US 1997-996343. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of treating cancerous cell growth mediated by raf kinase is being claimed in US 1997-996343 with a genus of the instant compounds of formula I whereas a method of treating cancerous cell growth with a subgenus of the compounds found in the US 1997-996343 application is being claimed in the instant application. It would have been obvious to one of ordinary skill in the art to treat cancerous cell growth with a subgenus of the compounds found in US 1997-

996343 application that are used to treat cancerous cell growth mediated by raf kinase. Accordingly, the method of treating cancerous cell growth with the instant compounds is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed method over those of the US 1997-996343.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 80 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. US 1997-996343. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application is claiming a method of treating cancerous cell growth mediated by raf kinase with a subgenus of the compounds found in US 1997-996343.

The difference between the US 1997-996343 method and the instantly claimed method is the teaching of a method of treating cancerous growth mediated by raf kinase

with a generic compound versus a subgenus of compounds. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds that are used in a method to treat cancerous cell growth mediated by raf kinase. Accordingly, the instant method is deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed method over those of the US 1997-996343 method of treating.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37 and 42, 43, 46 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 37 of copending Application No. 1997-996343. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds of formula I are a subgenus of the compounds claimed in the Application No. 1997-996343. The difference between the prior art compound and the instantly claimed compounds is the teaching of a generic compound versus a disclosed species. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus

to prepare structurally similar compounds. For instance, see the compound 1 of Table 1, page 80, where a disclosed species is exemplified. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 37 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 48 of copending Application No. Application No. 1997-996343. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9,11,12, 13,15,16 rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for all cancerous cell growth or all cancerous cell growth mediated by raf kinase or R1 of the compound

of formula in claim 1 equal to any C1-13 heteroaryl moiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment of raf mediated diseases with the compounds of formula (I) as found in claim 1.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. There are different cellular mechanisms, the unpredictability in the art and the different treatment protocols for the various types of cancers. Raf Kinase is but one pathway by which some cancers are mediated. Raf kinase activity and its inhibition has been correlated with a variety of human tumour types. (Monia et. al., Nat. Med. 1996, 2, 668-75, See Reference V).

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is found on pages 112-114 which discloses the raf Kinase assays of the compounds. Specific experimental data for the effect of the claimed compounds on cancerous cell growth and cancerous cell growth mediated by raf kinase is not disclosed.

The breadth of the claims

The breadth of the claims is the treatment of all cancerous cell growth and cancerous cell growth mediated by raf kinase with the compounds of formula I in claim 1.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the treatment of all cancerous cell growth and cancerous cell growth mediated by raf kinase and when faced with the unpredictability of the cancer therapy art.

The level of the skill in the art

Even though the level of skill in the cancer therapy art is very high, based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims and lack of guidance and direction for the treatment of all cancerous cell growth and cancerous cell growth mediated by raf kinase, one skilled in the art could not use the claimed invention without undue experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.

BMR

CEILA CHANG
PRIMARY EXAMINER
GROUP 1200/1625